are also downregulated. MSCs cultured on the embedded-fiber, soft matrix exhibit many similarities to cells on rigid substrates: higher SMA but lower collagen type I protein expression. Phosphorylation at serine-1943 (S1943) of non-muscle myosin IIA, which deactivates stress fiber assembly, is decreased on both fibrosis-like and rigid substrates but almost twice higher on a soft substrate. TGFβ is found to induce S1943 phosphorylation and SMA and collagen type I production. Surprisingly, inhibition of the TGFβ pathway perturbs matrix expression but not SMA, suggesting a response that is unique from those of myofibroblasts. Furthermore, these 'myo-MSCs' hint that, unlike myofibroblasts, they do not become hyper-contractile. This supports the notion that MSC engraftment into wounded tissues suppresses fibrosis, highlighting the promise of these cells in restoring normal tissue function.

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Modeling Scale-Up of Adherent Cell Cultures on Microcarriers via Bead to Bead Transfer

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As cell-based therapy is increasingly becoming a reality there is a need to generate large number of cells (10-12 billions) with small volume footprint and rapidly. One of the ways to realize this is to grow cells on microcarriers where cells adhere to microcarriers and then start doubling on the surface. Here we present a mathematical model that captures various aspects of cell growth on these surfaces. Specifically we present details of two models (i) continuum model that helps us determine cell specific and surface specific parameters from experimental data of cell growth on flat surfaces and (ii) discrete model that provides information on number of occupied sites and inhibited sites at an individual bead level. Further the discrete model captures some interesting aspects of cell scale up related to bead to bead transfer of cells. The model evaluates different scenarios like bead size, bead size to cell size, initial cell seeding and distribution of seeding and further evaluates if mixing could potentially enhance cell scale up.

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Theoretical-Experimental Studies of Electric Field-Induced Cell Responses

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Tissue injury results in induction of endogenous electric field (EF) that mediates biophysical interactions in the ionic wound environment, which play a crucial role in tissue repair. Externally applied EF may therefore provide a promising therapeutic approach for wound healing; however, information on EF-cell interactions in the wound is limited. This research presents a combined theoretical-experimental approach to study EF interactions with fibroblasts (FBs) in vitro. The cell is modeled as a membrane-enclosed hemisphere surrounded by electrolyte. Maxwell's equations are solved numerically (ANSYS-HFSS) to obtain 3D EF distribution inside and near the cell subjected to an externally applied EF. Experimentally, FBs were exposed to the EF in a parallel-plate capacitor for 72 hours; cell morphology, proliferation and expression of pro-angiogenic growth factors were assessed. Theoretical results demonstrate the spatially-varying EF distribution in the cell membrane, where induced potential may be sufficient to regulate voltage-gated ion channel activation. Cell exposure to the EF resulted in significantly increased expression of placenta growth factor but no change in other parameters. Ongoing studies will determine the role of EF-mediated activation of voltage-gated channels in the cellular response, contributing to development of EF-based therapies for tissue repair.

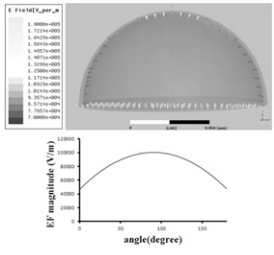

Figure 1. External EF induces intracellular electrical field distribution in the cell (3D-top, Angular distribution of the field on the membrane-bottom)

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Improving Longevity of Fibrin Sealant in a Proteolytic Environment

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Fibrin sealants are used in surgical procedures as an adjunct to sutures and staples to prevent fluid leakage and bleeding. These applications require extended longevity of fibrin sealant. It takes about 2 weeks for a typical surgical wound to heal, whereas fibrin sealant typically survives only 2 to 3 days *in vivo* due to its degradation by proteases such as plasmin present in the tissue microenvironment. Tranexamic acid (TA) is a well-known inhibitor of proteases including plasmin present in the blood. However, water soluble TA rapidly diffuses out of the sealant under *in vivo* conditions. Therefore, an investigation aimed to study the mechanism of sustained release of TA has been undertaken using microspheres of an absorbable PLGA (poly-lactic-glycolic-acid) polymer. TA particles of average dimension 3 micron are impregnated at a loading of 5% and 30% in average 40 micron PLGA microspheres. These are verified by Scanning Electron Microscopy / Energy Dispersive X-Ray spectroscopy. Confocal Raman spectroscopy shows that TA is distributed desirably more towards the core of the microsphere. Release study of TA by LC-MS using direct auto-sampler injection into Mass Spectral detector with ESI MS positive ion mode ionization shows that about 70% of TA from 5% TA Loaded / PLGA microspheres is released continuously over a period of 144 hours (or 6 days). Rate of TA release significantly slows down after the initial 72 hours. A gravimetric *in vitro* method has been developed to monitor the degradation of the sealant in a plasmin containing medium at pH 7.4 and 37 ^{0}C. The plasmin medium has been changed each day continuously up to 4 days. The proof-of-principle of improving longevity of fibrin sealant has been demonstrated with both 5% and 30% TA loaded / PLGA microspheres compared to the control.

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Robust High Performance Aquaporin based Biomimetic Membranes

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Aquaporins are water channel proteins with high water permeability and solute rejection, which makes them promising for preparing high-performance biomimetic membranes. Despite the growing interest in aquaporin-based biomimetic membranes (ABMs), it is challenging to produce robust and defect-free ABMs that can be easily scaled up. We have constructed robust thin film composite (TFC) ABMs with surface areas up to 600 cm^2 prepared by interfacial polymerization where Aquaporin Z-containing proteoliposomes were added to a m-phenylene-diamine aqueous solution thereby creating a polymer-rich film on top of a support membrane. Control membranes, either without aquaporins or with the inactive AqpZ R189A mutant aquaporin served as controls. The separation performance of the membranes was evaluated by cross-flow forward osmosis (FO) and reverse osmosis (RO) tests. In RO the ABM achieved a water permeability of ~ 4 L/(m^2 h bar) with a NaCl rejection $>$ 97% at an applied hydraulic pressure of 5 bar. The water permeability was ~40% higher compared to a commercial brackish water RO membrane (BW30) and an order of magnitude higher compared to a seawater RO membrane (SW30HR). In FO, the ABMs had $>$ 90% rejection for urea and a water permeability around 10 L/(m^{2}h) with 2M NaCl as draw solution. Our results demonstrate the feasibility of using aquaporin proteins in biomimetic membranes for technological applications.

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Membrane Protein Synthesis in Giant Vesicles

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Interest in the development of biomimetic cell models is driven by its potential to go beyond a purely descriptive picture of cellular processes towards a quantitative understanding and rigorous validation of theoretical modeling. Cells are exceptionally complex entities with a large variety of active and passive components. A quantitative investigation of a specific process in such complex environment is prohibitively challenging. In a biomimetic system like a giant unilamellar vesicle on the other hand the key components of a specific process can be studied isolated from other factors. In this way, it is possible to achieve quantitative information and that will allow us to discover the governing principles of the processes involved.

Recently we introduced a protocol to prepare advanced cell models from giant unilamellar vesicles for studies of membrane processes that involve transmembrane proteins. We further showed that specific functionalization permits to use those biomimetic systems in a lab-on-a-chip scenario. [1] Building on this development, we present here a novel approach that allows us to realize a mimetic cell model that includes in situ protein synthesis and active membrane translocation. Giant unilamellar vesicles were prepared starting from eukaryotic cell lysates containing both the eukaryotic protein synthesis machinery as well as the translocon that is required to integrate proteins into membranes. Our soft methodology for vesicle preparation on agarose-coated surfaces allowed us to keep the translocon fully functional. The advantage of in situ expression